REMARKS

Applicant respectfully requests reconsideration of the present application in view of the reasons that follow.

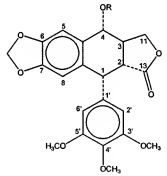
This response does not add, change or delete claims in this application. Claims 1, 8, 13-15, 22-24, and 57-59 are now pending in this application.

Allowable Subject Matter

Applicant thanks the examiner for her reconsideration of the application and withdrawal of all rejections under 35 U.S.C. § 103. Applicant is confused by the indication of allowable claims on the Office Action Summary and within the Action itself. The Office Action Summary indicates that claims 13, 29 and 57 are allowed. On the other hand, page 5, paragraph 7, of the Office Action indicates that claims 13 and 57-59 are allowed. Since claim 29 is not pending in the present application and the Examiner's substantive statements are addressed to claims 13 and 57-59, Applicant understands that claims 13 and 57-59 are allowed.

35 U.S.C. § 112, first paragraph – enablement

Claims 1, 8, 14, and 22-24 stand rejected under 35 U.S.C. § 112, first paragraph, as filing to comply with the enablement requirement. Claim 1, the independent claim, is drawn to a compound represented by the formula:



wherein R is C§-$(CH_2)_m$-X-R_1, wherein m is 0-10, X is a covalent bond, and R_1 is optionally substituted, unsaturated or partially saturated, 6-membered heterocycle. Claims 8, 14, 22-24

depend on claim 1. In particular, claim 14 recites compounds wherein R_1 is an optionally substituted 6-membered heterocycle with one or two nitrogens in the ring.

The Office Action states that the claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. In particular, the Action asserts that the specification is not enabling for R_1 being optionally substituted, unsaturated or partially saturated, 6-membered heterocycle and R_1 is 6-membered heterocycle with one or two nitrogens. Office Action at 3. Citing *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) for factors to determine whether any necessary experimentation is undue, the Office Action asserts that a skilled artisan would expect the claimed compounds with 6-membered heterocycles containing O, S and N atoms to behave differently and that "[a] slight change in structure of the compounds could dramatically change its biological activity in vitro" and in vivo. Office Action at 2-3. The Action thus concludes that Applicant has "not shown compounds commensurate in scope with the claimed invention effective treating colon cancer" because only the thymin-1-yl species is disclosed. Office Action at 3.

In order to make an enablement rejection, the Office has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, (Fed. Cir. 1993). "It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971). Applicant submits that the Patent Office has not met its burden in establishing the instant rejection.

In the instant case, the specification teaches that the R_1 group of the podophyllotoxin derivatives can have a wide scope of structure diversity without destroying the anti-tumor activity. More than twenty examples of podophyllotoxin derivatives having a variety of R_1 groups are disclosed. The R_1 groups include phenyl groups with substitutions such as halo (*See,*

e.g., Examples 1A – 4A), aldehyde (Example 6A), methoxy (Example 7A), substituted amino group (Example 10A), or a combination of substituents (Examples 5A and 8A); heterocyclic moieties having oxygen atom§, such as coumarin (Example 9A), furan (Example 13A), chromone (Example 12A), anthraquinone (Example 14A); and heterocylic moieties having nitrogen atom(s), such as quinoline (Example 15A), thymine (Example 16A), and tetrahydro-β-carboline (Example 22). Table 1 shows that each of these compounds exhibits activity comparable to that of etoposide (a derivative of podophyllotoxin having an oxygen-containing bicyclic heterocycle at the position corresponding to R of the present claims) in inhibiting cell growth in vitro. These results indicate that anti-tumor activity is well preserved in podophyllotoxin derivatives with a wide structure diversity at the R_1 position. Thus, based on experimental data provided in the specification, one of ordinary skill in the art would have every expectation that the claimed compounds would be useful for treating breast or colon cancer.

Indeed, such a conclusion is entirely consistent with the Examiner's own statements. In allowing claims 13 and 57-59, the Examiner states:

> The prior art neither teaches nor suggests the claimed compounds. In the absence of any evidence or apparent reason why the claimed compounds do not possess the disclosed utility, the allegation of utility in the specification must be accepted as correct. In re Kamal et al. 158 USPQ 320; Ex parte Krenzer, 199 USPQ 227.
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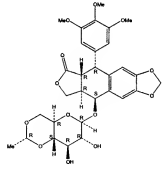
> Mantle, Therapeutic applications of medicinal plants in the treatment of breast cancer: a review of their pharmacology, efficacy and tolerability, PMID: 11059361 (2000) teach Etoposide well recognized to treat breast cancer.



> Etoposide has the above formula. One of ordinary skill in the art would expect compounds structurally to have similar properties. Thus the claimed compounds would be expected to be useful to treat breast or colon cancer.

The analysis presented for claims 13 and 57-59 applies equally to the compounds of claims 1, 8, 14, and 22-24. Each of these claims is drawn to derivatives of podophyllotoxin having a substituted, unsaturated or partially saturated, 6-membered heterocycle rather than the hydroxy-substituted saturated bi-cyclic heterocycle of etoposide. As stated by the Examiner, "one of ordinary skill in the art would expect compounds structurally similar to have similar properties." In the absence of evidence to the contrary, the rejection for lack of enablement cannot stand.

The Office Action apparently has ignored the broad scope of the teachings provided in the specification regarding the entire genus when it states that only the thymin-1-yl species is disclosed. The Action states that a skilled artisan would expect the activity of the compounds be dramatically different if the structure of the compounds change slightly. Applicants submit that such assertion when applied to the claimed compounds is without basis and is in conflict with the teachings of the specification. Further, the statement is inconsistent with the Examiner's reasoning in allowing claims 13, 57-59, where the Examiner states that compounds claimed in claims 13, and 57-59 are useful to treat breast or colon cancer based on their structural similarity with etoposide because one of ordinary skill in the art would expect compounds structurally similar to have similar properties. Office Action at 6. Applicants submit that compounds claimed in claims 1, 8, 14, 22-24 also possess structural similarity with etoposide as well as with the compounds disclosed in the Examples. Thus, the use of the claimed compounds in claims 1, 8, 14, 22-24 to treat breast cancer are enabled by the specification.

Therefore, the Office Action has not established a prima facie case of lack of enablement for Applicant to rebut. Accordingly, Applicant respectfully requests that the rejection be withdrawn.

35 U.S.C. § 112, first paragraph – written description

Claims 1, 8, 14, 22-24 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to comply with the written description requirement. The Office Action asserts that the claims contain subject matter—R_1 being an "optionally substituted, unsaturated or partially saturated, 6-membered heterocycle" or being a "6-membered heterocycle with one or two nitrogens in the ring"—"that was not described in the specification in such a way to convey reasonably to one skilled in the relevant art that the inventor(s), at the time of the application was filed, had possession of the claimed invention." Office Action at 3. The Office Action states that the term encompasses groups a description of which is not found in the specification. In making such a conclusion, the Office Action cites *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), *in re Smythe*, 480 F.2d 1376, 1383, (CCPA 1973), and MPEP §§ 2163, 21.63.02. office action 4. Applicant respectfully traverses the rejection.

The test for written description requirement is whether an applicant conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention claimed. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). The written description requirement for a chemical genus "requires a precise definition, such as by structure, formula, or chemical name," of the claimed subject matter sufficient to distinguish it from other material. *Eli Lilly*, 43 USPQ2d at 1406. MPEP § 2163(II)(3) states that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Applicant submits that the claimed subject matter satisfies the written description requirement under the standard articulated above. The rejected terms themselves are structural description of the genus. They describe that the R_1 group of formula I can be an optionally substituted, unsaturated or partially saturated, 6-membered heterocycle or more narrowly an

optionally substituted 6-membered heterocycle with one or two nitrogens in the ring. These terms appear in claims 1, and 14 as originally filed and in the specification, *see e.g.* page 2, line 5, page 9, line 6 (optionally substituted 5-or 6-membered heterocycle). The term 6-membered heterocycle is described to be a "monovalent radical of a 6-member closed ring containing carbon and at least one other element, generally nitrogen, oxygen, or sulfur and may be fully saturated, partially saturated, or unsaturated." Specification, page 7, lines 9-11. Therefore compounds with R_1 being an optionally substituted, unsaturated or partially saturated, 6-membered heterocycle or more narrowly an optionally substituted 6-membered heterocycle with one or two nitrogens in the ring were encompassed by the description. Thus, there is sufficient description of the structure of genus that would allow a skilled artisan to understand that Applicant had possession of the genus. The description also clearly distinguishes the claimed genus from other materials, such as compounds where R_1 is piperidinyl, which was cited as prior art in the July 20, 2005 Office Action.

The Office Action, however, rejects the claims because only a single thymin-1-yl species was disclosed. The Office Action apparently equates "written description" to "reduction of practice." Reduction to practice is only one of the methods to satisfy the written description requirement. *See* MPEP § 2163(II)(3). As stated above, Applicant submits that the written description requirement is satisfied because there is sufficient structural description of the whole 6-membered heterocycle genus although only the thymin-1-yl species was reduced to practice.

The Office Action also asserts that "Applicants' functional definitions in the claimed formula simply lack of precision required by the Court of Appeals for the Federal Circuit." The office Action cites *In re Smythe*, 480 F.2d 1376, 1383, (CCPA 1973) which states that "[i]n other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus or combination claimed at a later date in the prosecution of a patent application."

Applicant respectfully submits that the description of the claimed formula is not merely functional as stated by the Examiner, but rather structural description. There is no functional language in the claim or in the compound aspect of the invention. Applicant further submits that the statement of *Symthe* is inapplicable to the instant case. The applicants in *Symthe* attempted to broaden claims to encompass subject matter not described in the specification and original claims. *Symthe*, 480, F.2d at 1378. The court held that in that particular case, this was allowed because the broader subject matter was conveyed to one skilled in the art. *Id.* at 1383. However, the court cautions that where there is unpredictability, one skilled in the art may not be placed in possession of a genus "claimed *at a later date* in the prosecution of a patent application." *Id.* (emphasis added). Thus, the *Symthe* court was trying to restrict claiming of subject matter that was not disclosed in the specification as originally filed. In the instant case, however, Applicant does not attempt to broaden any claims to encompass subject matter not disclosed in the specification and original claims. As described above, all claimed subject matter has support in the originally filed application.

For the above reasons, Applicants respectfully request that the Examiner withdraw the lack of written description rejection against claims 1, 8, 14, 22-24.

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely

acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date 8 December 2006

By _____

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